



There is an art to science, and science in art;
the two are not enemies, but different aspects of the whole.

Isaac Asimov, 1988

Forum

Breast Cancer and MCS in EHP

In recent years, much progress has been made in understanding why certain women develop breast cancer, and several studies have proposed that environmental factors can significantly affect a person's likelihood of the disease. Despite these advances, the mechanisms underlying cancer largely remain a mystery. Similarly, many researchers have suggested that the recently diagnosed phenomenon known as multiple chemical sensitivity (MCS) could be caused by exposure to environmental toxins, but how these chemicals enter the body and cause such a reaction remains a mystery. *EHP* will publish two monographs containing important research on these subjects, *Experimental Approaches to Chemical Sensitivity* in March 1997 and *Hormones, Hormone Metabolism, and Breast Cancer* in April 1997.

MCS is a poorly understood condition in which patients have severe reactions to chem-

icals in concentrations that most people can easily tolerate. Perfumes, household cleaners, and petroleum-based products have been reported to cause illness in some patients suffering from MCS. Chemicals, however, do not always trigger the same responses among different MCS patients and, although some patients have reported past exposure to a known toxicant that coincided with the onset of MCS, others can report no such exposure, making the condition difficult to characterize and diagnose.

Clinical ecologists have long suggested that exposure to low levels of chemicals can cause physiological responses in genetically susceptible persons including illnesses such as cancer and arthritis. On the other hand, in an attempt to distinguish the condition from known occupational diseases and psychiatric conditions, the occupational health literature has provided a definition of MCS as a novel condition that could possibly be acquired through classic conditioning. Each approach

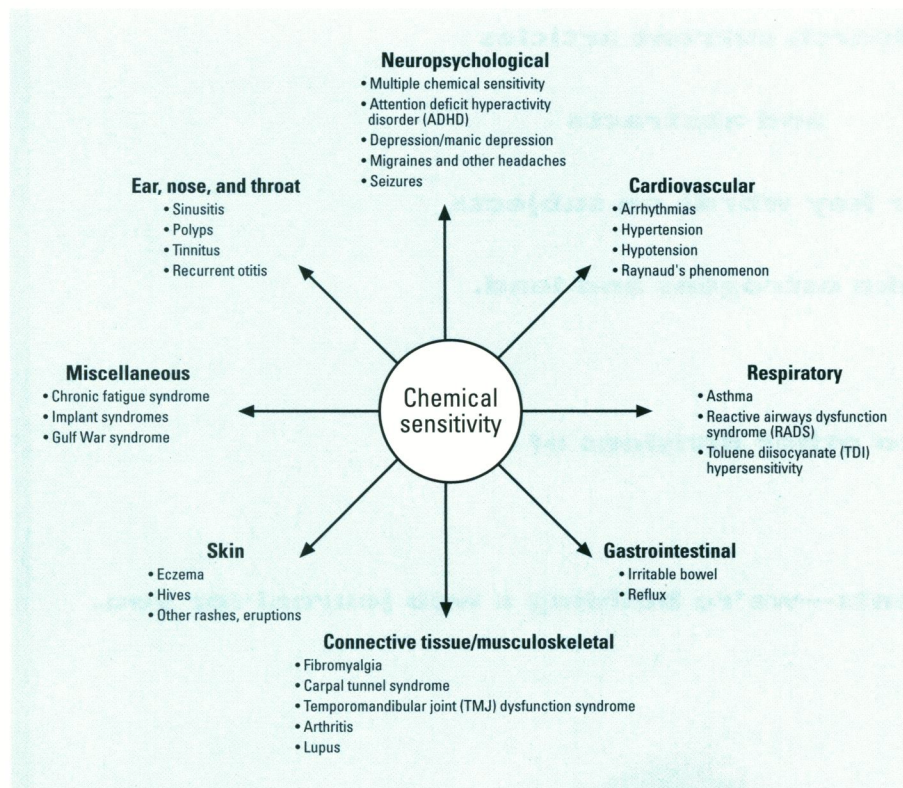
carries different implications for how MCS should be studied and what kind of treatments are likely to be effective.

"If this is a purely psychological phenomenon—that is, one that is conditioned—then it can be learned or unlearned," says Nancy Fiedler, associate professor in the Environmental and Occupational Health Sciences Institute of the Robert Wood Johnson Medical School, who led the MCS workshop that prompted the MCS monograph. "On the other hand, others would suggest that we need to extend the dose-response curves to include physiological responses that can be brought on by very low doses. These are responses that cannot be unlearned . . . through psychiatric therapy."

Other researchers disagree with the notion that MCS can be effectively studied as either a purely psychological or purely physiological phenomenon. Some have suggested that stress must accompany a toxic exposure to initiate sensitivity. Others propose that an initiating exposure can affect the physiology of the brain through a process similar to the limbic kindling seen in animals, through which intermittent low-level stimuli can cause the brain to change so that further stimulus will initiate full-blown seizures. According to Iris Bell, director of the Geriatric Psychiatry program at the Tucson Veterans Affairs Medical Center, "The mind versus body conceptualization of MCS is extremely erroneous." Bell says that a better understanding of the field of psychology would allow researchers to better understand MCS as a complex mind-body interaction.

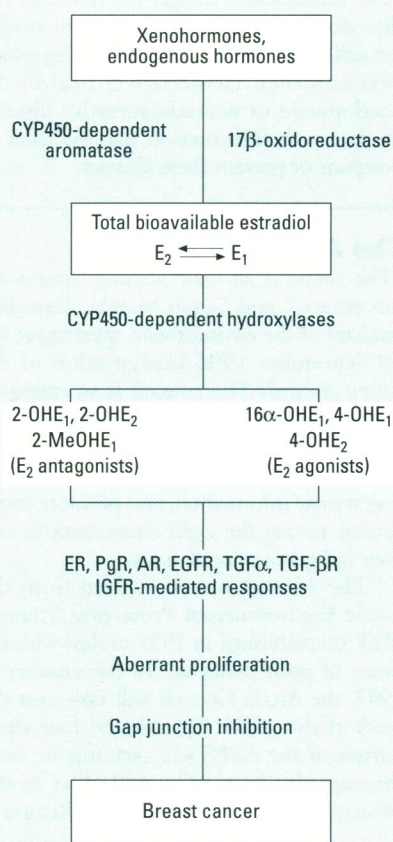
Experimental Approaches to Chemical Sensitivity attempts to provide a basis for comparing the different approaches toward MCS in hopes of developing a unified research strategy. Some papers in the monograph deal with clinical case studies that describe various symptoms and characteristics of MCS patients. Other papers propose models for MCS, describing the condition as related to the learning process, to time-dependent sensitization, or to the mechanisms underlying drug abuse. Still others suggest experimental methods and variables that could be employed in experimental studies of MCS.

Hormones, Hormone Metabolism, and Breast Cancer is dedicated to the issues of breast cancer and the effects of hormones on



The mystery of MCS. Characterizing multiple chemical sensitivity is made difficult by the broad range of symptoms associated with it.

Source: Miller CS. Toxicant-induced loss of tolerance—an emerging theory of disease? *Environ Health Perspect* 105(suppl 2):445-453 (1997)



Hormones and breast cancer. Steroid hormone metabolites having estrogenic or antiestrogenic properties exert their growth modulatory effects indirectly via receptor-mediated mechanisms, leading to aberrant proliferation and breast cancer.

Source: Davis DL, Telang NT, Osborne MP, Bradlow HL. Medical hypothesis: bifunctional genetic-hormonal pathways to breast cancer. *Environ Health Perspect* 105(suppl 3): 571-576 (1997)

the development of this disease, the most common cancer among women. An October 1993 petition signed by 2.6 million people asked President Clinton for a new strategy to fight breast cancer. This petition led to the development of the National Action Plan on Breast Cancer (NAPBC). The Etiology Working Group of the NAPBC, together with the National Cancer Institute, Tulane University's Center for Bioenvironmental Research, and the U.S. Public Health Service's Office of Women's Health convened a workshop on hormones and breast cancer 28-29 September 1995. Selected papers from this workshop, as well as some response papers, form the basis of *Hormones, Hormone Metabolism, and Breast Cancer*.

Modern epidemiological studies have found that most of the known risk factors for breast cancer, excluding radiation, are directly related to lifetime exposure to estradiol and other hormones. Researchers have reasoned that any environmental chemical that has the ability to mimic human hormones or affect their metabolism may be

carcinogenic. However, some xenohormones (such as DDT) appear to be harmful, while others (such as phytoestrogens) appear to be protective. The mechanisms by which xenohormones influence bodily processes, potentially leading to cancer, have not been decisively identified. The papers presented in *Hormones, Hormone Metabolism, and Breast Cancer* contribute to elucidating these mechanisms and differentiating among helpful and harmful hormones.

The monograph also includes views and concerns of some breast cancer research advocates. For example, Sandra Steingraber of the Women's Community Cancer Project writes about her concern that more work is being done to identify the mechanisms of cancer than is being done to protect the public from the disease. "We are interested in research that identifies breast carcinogens, and we [are also] interested in social changes that would keep these agents out of women's breasts in the first place," says Steingraber. In another paper, Craig Dees of the Oak Ridge National Laboratory and colleagues propose that the colorant Red Number 3 causes genetic damage and could be a significant risk factor for breast cancer.

Other researchers present additional support for a link between sex hormone levels and breast cancer incidence. One nested case-control study by Joanne F. Dorgan of the National Cancer Institute and colleagues examines serum estrogen levels and cancer incidence in postmenopausal women. Another paper finds that dietary estrogens at low concentrations can stimulate human breast cells to begin replication. In a paper by Ruth H. Allen of the National Cancer Institute and colleagues, the relationship between increasing breast cancer incidence among women in Hawaii and the use of pesticides there provides evidence of a link between xenohormones and cancer risk.

Research on the link between known risk factors for breast cancer and lifetime exposure to bioavailable estradiol has led to the idea that xenohormones can affect the body by two distinct paths, either by attacking DNA directly or by interacting with endogenous hormones and altering the formation of hormone metabolites. A paper by Takeki Tsutsui of the Nippon Dental University and colleagues found evidence of DNA adduct formation and aneuploidy induction

(precursors to cancer) in response to estrogen. The mechanism by which phytoestrogens may work to prevent cancers is discussed in *Hormones, Hormone Metabolism, and Breast Cancer*, and monograph authors suggest that these chemicals act to reduce the binding of other xenoestrogens to human estrogen receptors. It is also suggested in the monograph that the presence or absence of lipophilic regions on estrogens and xenoestrogens may affect their binding characteristics and could be used to distinguish harmful estrogens from beneficial ones.

The papers presented in *Hormones, Hormone Metabolism, and Breast Cancer* also discuss ways of measuring human hormone levels as a means of assessing an individual's risk of developing breast cancer. Researchers compared the sensitivity of two competing methods of measuring hormone metabolites (2-hydroxyestrone and 16α-hydroxyestrone immunoassays) and found a high degree of agreement for premenopausal women, a finding that could lead to more refined methods of measurement. Other authors identified ways to measure xenoestrogen levels in human serum. According to Devra Davis, program director of the Health, Environment, and Development Program of the World Resources Institute and an editor of the monograph, better methods of measuring hormone levels will make it easier for scientists to identify environmental carcinogens. "Experimental methods for identifying hazards need to be developed, and measuring [xenohormone] levels present [in the body] is a very direct way of assessing exposure." Davis said that future research should concentrate on these issues.

New Dimensions to Dementia

Two studies published last September provide new clues to possible links between environmental factors and neurodegenerative diseases. Both genetic and environmental factors are thought to play a role in the development of such diseases. However, until now, "more progress has been made on the genetic side of the equation," says George Martin, director of the Alzheimer's Disease Research Center at the University of Washington in Seattle. These studies and others like them are the latest attempts to rectify that imbalance.

The first study, published in the 25

